

Application For Research Grant

Date: November 23, 1954

*out of my field
could be good
define "tobacco products"*

1. Name of Investigator: **Bernard M. Wagner, M.D.**
2. Title: **The Effect of Tobacco Derivatives on the Ground Substance**
3. Institution & Address: **Hahnemann Medical College and Hospital
235 North 15th Street
Philadelphia 2, Pennsylvania**
4. Project or Subject: **Relationship of tobacco products to vascular disease.**

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5. Detailed Plan of Procedure (Use reverse side if additional space is needed):

Attention has again been centered on the adverse effects of smoking on the cardiovascular system. The exact nature of this phenomenon is not clear. It is well known that certain peripheral vascular diseases are made worse by smoking and may accelerate ~~xxxx~~ vascular occlusive events.

The earliest changes in blood vessels observed microscopically is a "thickening" of the intima. This covers a diverse range of events but in almost all vessels studied from patients with collagen disease, the first noticeable alteration is an accumulation of intimal ground substance. Following this change, a protein-rich material collects which is usually described as "hyaline" or "fibrinoid". Since the ground substance is intimately related to fibroblastic activity and circulating proteins, it becomes evident that these factors are worthy of study.

Investigations in this laboratory concerning the ground substance in the vessels of patients with generalized scleroderma, disseminated lupus erythematosus, malignant hypertension and acute rheumatic fever, have shown that the fibrinoid material present in each case is not identical. Thus, tinctorial similarity does not denote identity. In rheumatic fever, the collagen fibers are directly involved while in malignant hypertension the fibrinoid substance appears to be derived from the muscle.

Fibroblasts actively growing in tissue culture would serve as an ideal source of cells and ground substance. Pilot experiments (Mount Sinai Hospital, New York) have shown that mucopolysaccharides collect in the tissue culture liquor. Various tobacco products in solution would be applied to these cultures. These would then be studied for cytopathological changes and the culture media analyzed chemically for changes in protein-carbohydrate complexes. Cultures will be grown on thin pieces of sponge so that they can be fixed and sectioned. The sections will then be studied by histochemical methods to note any changes in the functional ability of the cells.

6. Budget Plan:

Salaries - Chemist, full time (Ph.D.)	\$5,500
Expendable Supplies	3,000
Permanent Equipment	3,000
Overhead	920 (8%)
Other	
Total	\$12,420

7. Anticipated Duration of Work: 12 to 18 months

8. Facilities and Staff Available:

Staff: Bernard M. Wagner, M.D., Assistant Professor of Pathology, in charge of Experimental Pathology

V. N. Damodaran, M.D., Instructor in Pathology

H. T. Segura, M.D., Research Fellow in Pathology

K. C. Pani, M.D., Research Assistant in Pathology

Sylvia Shapiro, Research Histopathology Technician

Facilities

Histochemistry Laboratory

Space for tissue culture laboratory

9. Additional Requirements: Animal Laboratory

Radioisotope Laboratory

10. Additional Information (Including relation of work to other projects and other sources of supply):

At present, the Section of Experimental Pathology is being supported by grants from the Heart Association of Southeastern Penna., Office of the Surgeon General, U. S. Army and the Cardiovascular Institute, Hahnemann, Hospital. The problem under investigation concerns the nature of the ground substance in rheumatic fever. Histochemical, cytochemical, microchemical and biophysical methods are being used. The methods now established will allow for a comprehensive study of the effects of tobacco products on the pathogenesis of vascular disease. In addition to the vascular maladies previously mentioned, atherosclerosis will also be studied in the experimental animal. Tissue cultures from atherosclerotic rabbit aortas will be investigated as to the effects of tobacco products.

Signature

Director of Pathology, Bernard M. Wagner

Business Office, Joseph J. Hayes, Jr.

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